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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,518	02/27/2004	Joan S. Steffan	00047	7728

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EXAMINER	
DUTT, ADITI	
ART UNIT	**PAPER NUMBER**
1649	

MAIL DATE	DELIVERY MODE
07/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,518	STEFFAN ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. The amendment filed on 10 April 2007 has been entered into the record and has been fully considered. Claim 19 is amended. Claims 1-18 and 20-77 are canceled.

2. Claim 19 drawn to a method of treating Huntington's Disease (HD) in a patient by administration of a therapeutically effective amount of a small ubiquitin-like modifier isopeptidase, are under consideration in the instant application.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on 10 April 2007, have been fully considered. New grounds of objection and rejection are as follows.

Response to Amendment

Withdrawn objections and/or rejections

5. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (10 April 2007).

6. Upon consideration of the amendment to claim 19, and the cancellation of all other claims, rejection of claims 19-20, 33-35, 44 and 50, under 35 USC § 112, second paragraph is withdrawn.

Claim rejections/objections maintained/new grounds of rejection

Claim objection

7. Claim 19 is objected to because of the following information: Regarding claim 19, the term 'enhancer' is not crossed off on the last line of the amended claim. Appropriate correction is required.

35 U.S.C. § 112, first paragraph – Lack of enablement

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Applicant argues that the Examiner is wrong in citing a generic statement in Wang's reference, that points out to the insufficiency of the Drosophila model for the treatment of polyglutamine expansion related neurodegeneration. Applicant argues that this assertion is not true as evidenced from Wang et al and other contemporaneous references. For example, Applicant quotes Wang et al's statement, which suggest that flies "mimic human disease in every important way". Furthermore, Applicant cites Thompson and Marsh, that reiterate similar beliefs, that the Drosophila transgenic model of neurodegenerative disease such

as HD, are excellent models for exploring therapeutic strategies in humans. Applicant goes on to exemplify the importance of the transgenic fly in experiments for developing drugs for other neruodegenerative diseases. Applicant finally asserts that the working example of the fly is proper and commensurate to the claimed invention, and the Examiner's contention is unwarranted and improper.

10. Applicant's arguments directed to the claimed invention have been fully considered but have not been found to be persuasive. Examiner acknowledges that the Drosophila fly model is extensively used for studying different aspects of neurodegenerative diseases in humans and expresses genes that mimic the pathology in mammalian systems. Examiner also agrees that the Drosophila provides a "cost-effective platform for testing large matrices of drug combinations". However, Examiner does not agree with the Applicant's argument that the fly model can be used for determining a method of treatment of HD in humans. As stated in the last Office Action, and extensively argued upon by the Applicant, it is reiterated that for treatment purposes, "the proof of efficacy in mammalian models is considered as a prerequisite before considering possible testing in humans". The Drosophila model is more important as a pre-screen for testing and identifying drugs for the treatment, not for treatment *per se* of complex neurodegenerative diseases, like HD in humans. The citations provided by the Applicants in the instant response corroborate this assertion. For example:

Thompson and Marsh state that, ".....allow fly studies to speed the progress of identifying promising therapeutic strategies for testing in manmals" (emphasis added) (page 10).

Marsh et al. state that,
"Drosophila.....for testing large matrices of drug combination for optimal combinations of therapeutic drugs, and to test for undesirable interactions, before proceeding to mouse models or patients suffering from HD". ....(emphasis added) (page 11)

"Preclinical in vivo testing strategies such as those described here could result in a great savings of cost and time in developing potential disease treatments and can serve to identify treatment regimens that are very likely to provide therapeutic benefit to patients". (page 11).

Examiner agrees with Applicant's assertion that the fly has proven extremely effective at identifying effective strategies, which again proves that the fly is good model for identifying and testing therapeutics, not a model for the treatment of diseases. It is noted that there is a difference between testing or identifying treatment strategies and actually treating a human. As stated in the previous Office Action, it is reiterated, that to test for treatment of a disease in a subject, one would need to conduct studies on non-human mammals that would more closely replicate the essential features of the pathophysiology of the disease in humans, as compared to invertebrate models (page 9). Furthermore, as taught by Applicant provided reference (Melchoir, Ann Rev Cell Dev Biol 16: 591-626, 2000 – included in form 1449), several SUMO isopepdises such as SENP1..., etc., are localized in different subcellular regions (page 601-602). One skilled in the art would not be able to predict from the instant specification, that all possible

SUMO isopeptidases will be therapeutically effective in treating HD. Undue experimentation would be required to determine such.

11. Specifically, proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to treat HD by administration of any SUMO isopeptidase; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which has yet to determine an ideal model for treatment of Huntington's Disease and, the unpredictability of using invertebrate models for actual treatment in humans, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Status of Claims

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

14. A shortened statutory period for reply to this final action is set to expire

THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

17. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
18 June 2007

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
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